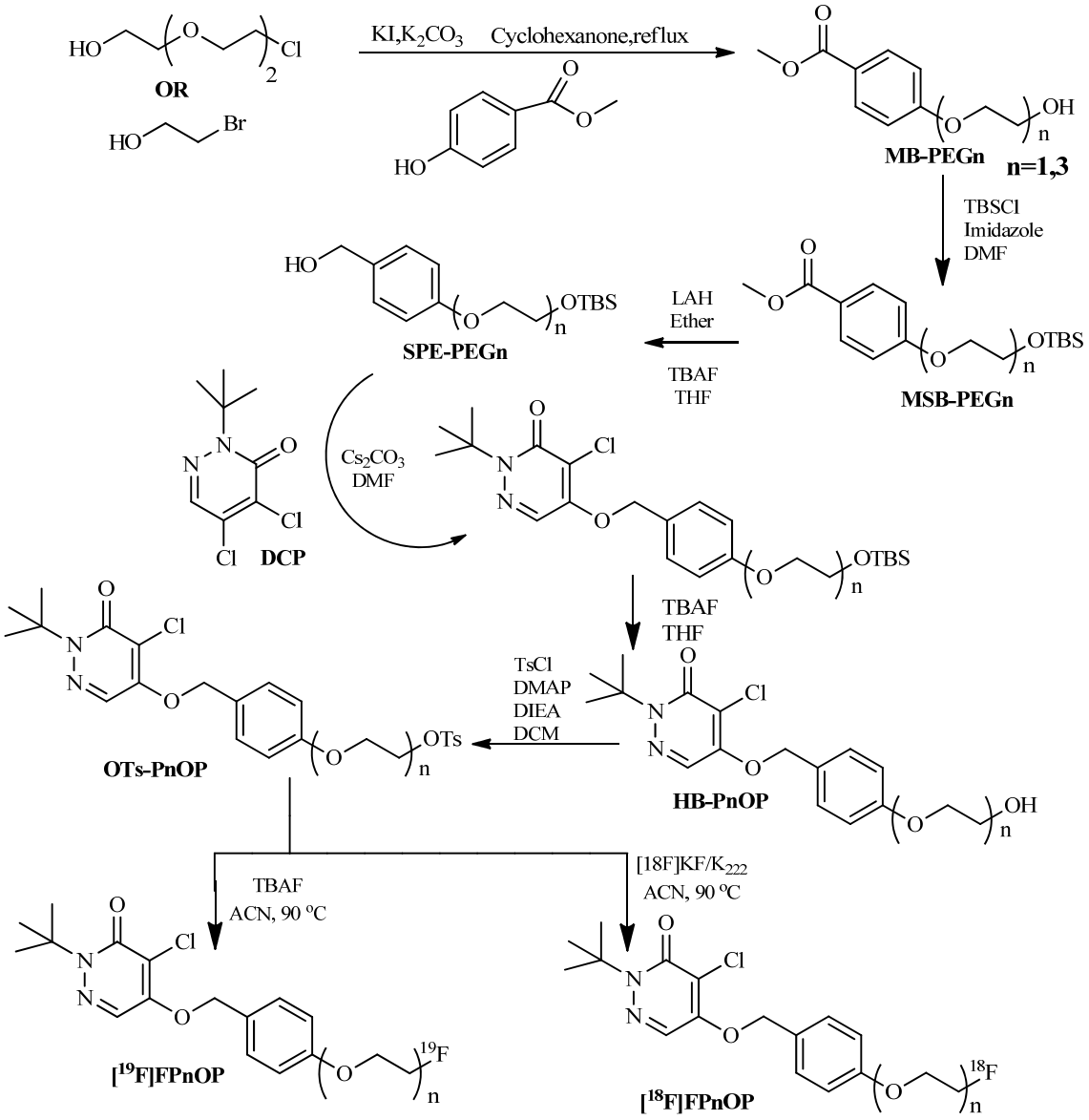
Supplemental data

1. Preparation of MB-PEGn (n=1, 3)

Cyclohexanone (5020 mL) was added to a mixture of methyl 4-hydroxybenzoate (3 g, 19.7 mmol, 1 equiv), KI (1.65 g, 9.8 mmol, 0.5 equiv), and K_2CO_3 (5.4 g, 39.4 mmol, 2 equiv) with stirring under nitrogen. 2-bromoethanol or 2-(2-(2-chloroethoxy)ethoxy)ethanol (1 equiv) was added into the reaction flask, and refluxed with stirring for 1 d under nitrogen. The suspension was cooled to room temperature and filtered to remove the solids. The yellow-orange filtrate was concentrated in vacuo. After that, CH_2Cl_2 (50 mL) was added to the residue, filtered, and the filtrate was concentrated in vacuo again. The residue was chromatographed over a column of silica gel and eluted with hexane and ethyl acetate = 2 : 3 (v/v) to give the MB-PEGn as buff oil (yield: 43% for MB-PEG1, and 50% for MB-PEG3).

^{1}HNMR f and IR or MB-PEG1: ^{1}HNMR (400 MHz, $CDCl_3$) δ: 3.821 (s, 3H, O*CH_3*), 3.930 (t, 2H, phenyl-O-CH_2*CH_2*), 4.074 (t, 2H, phenyl-O-*CH_2*), 6.870 (d, 2H, O-*phenyl*), 7.930 (d, 2H, CO- *phenyl*). IR (CH_2Cl_2 cm^{-1}) *v:* 3444 (O-H), 1718 (C=O), 1161 (C-O-C).

^{1}HNMR for MB-PEG3: ^{1}HNMR (400 MHz, $CDCl_3$) δ: 3.174 - 4.110 (m, 12H, O(C*H_2*C*H_2*O)$_3$H), 6.858 (d, 2H, O-*phenyl*), 7.895 (d, 2H, CO- *phenyl*).



Supplemental Figure 1. The synthesis route of OTs-PnOP, non-radioactive references [^{19}F]FPnOP and radiotracers [^{18}F]FPnOP (n=1, 3).

2. Preparation of MSB-PEGn (n=1, 3)

Anhydrous DMF (10 mL) was added into the mixture of imidazole (0.89 g, 12.9 mmol, 1.5 equiv), MB-PEGn (1 equiv) and tert-butyldimethylsilyl chloride (1.94 g, 12.9 mmol, 1.5 equiv). After stirring in an oil bath for 4 h at 80 °C, the reaction mixture was diluted with ethyl acetate (50 mL) and extracted five times with saturated NaCl solution (50 mL for each

extraction), then extracted two times with saturated $NaHCO_3$ (50 mL for each extraction). The organic phase was dried with $MgSO_4$, filtered, and concentrated under reduced pressure to give MSB-PEGn as buff oil (yield: 96% for MSB-PEG1 and 91% for MSB-PEG3).

^{1}HNMR and IR for MSB-PEG1: ^{1}HNMR (400 MHz, $CDCl_3$) δ: 0.000 (s, 6H, OSi*(CH$_3$)$_2$*), 0.808 (s, 9H, SiC*(CH$_3$)$_3$*), 3.8782 (s, 3H, O*CH$_3$*), 3.886 (t, 2H, phenyl-O-CH_2*CH$_2$*), 3.992 (t, 2H, phenyl-O-*CH$_2$*), 6.825 (d, 2H, O-*phenyl*), 7.882 (d, 2H, CO- *phenyl*). IR (CH_2Cl_2 cm^{-1}) *v*: 1722 (C=O), 1253 (=C-O-C), 1109 (C-O-C).

^{1}HNMR and IR for MSB-PEG2: ^{1}HNMR (400 MHz, $CDCl_3$) δ: -0.005 (s, 6H, OSi*(CH$_3$)$_2$*), 0.822 (s, 9H, SiC*(CH$_3$)$_3$*), 3.503 - 4.118 (m, 12H, O(*CH$_2$*C*H$_2$*O)$_3$Si), 6.866 (d, 2H, O-*phenyl*), 7.917 (d, 2H, CO- *phenyl*); IR (CH_2Cl_2 cm^{-1}) *v*: 1712 (C=O), 1254 (=C-O-C), 1059 (C-O-C).

3. Preparation of SPE-PEGn (n=1, 3)

The solution of MSB-PEGn (1 equiv in 15 mL ether) was dropped slowly into the mixture of anhydrous ether (20 mL) and $LiAlH_4$ (0.74 g, 19.4 mmol, 2 equiv), stirring in the ice bath for 2 h, then stirring for another 2 h at room temperature. The water was dropped slowly into the flask until no gas produced, and then the pH was adjusted to 6. After filtered, filtrate was dried with $MgSO_4$, filtered, and concentrated to give SPE-PEGn as buff oil (yield: 95% for SPE-PEG1 and 77% for SPE-PEG3).

^{1}HNMR and IR for SPE-PEG1: ^{1}HNMR (400 MHz, $CDCl_3$) δ: -0.005 (s, 6H, OSi*(CH$_3$)$_2$*), 0.807 (s, 9H, SiC*(CH$_3$)$_3$*), 3.865 (t, 2H, *CH$_2$*CH$_2$OSi), 3.927 (t, 2H, CH$_2$*CH$_2$*OSi), 4.497 (s, 2H, *CH$_2$*-O-C=C-Cl), 6.789 (d, 2H, O-*phenyl*), 7.171 (d, 2H, CO- *phenyl*). IR (CH_2Cl_2 cm^{-1}) *v:* 3341 (O-H), 1131 (C-O-C).

^{1}HNMR and IR for SPE-PEG2: ^{1}HNMR (400 MHz, $CDCl_3$) δ: 0.000 (s, 6H, OSi*(CH$_3$)$_2$*), 0.849 (s, 9H, SiC*(CH$_3$)$_3$*), 3.532 - 4.117 (m, 12H, O(*CH$_2$*C*H$_2$*O)$_3$Si), 4.584 (s, 2H, *CH$_2$*-O-C=C-Cl), 6.880 (d, 2H, O-*phenyl*), 7.246 (d, 2H, CO- *phenyl*). IR (CH_2Cl_2 cm^{-1}) *v:*

3431 (O-H), 1116 (C-O-C).

4. Preparation of SB-PnOP (n=1, 3)

Anhydrous DMF (10 mL) was added to the mixture of SPE-PEGn (1 equiv), DCP (5.02 g, 19.5 mmol, 3 equiv) and Cs_2CO_3 (6.35 g, 19.5 mmol, 3 equiv), and stirred for 12 h at 68 °C in an oil bath. After cooled to temperature, the reaction solution was diluted with ethyl acetate (50 mL), and washed five times by saturated NaCl solution (50 mL for each time). The organic phase was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was chromatographed over a column of silica gel and eluted with the mixture of hexane and ethyl acetate = 5 : 1 (v/v). After removal of the solvents under vacuum, SB-PnOP was obtained as buff oil (yield: 43% for SB-P1OP and 52% for SB-P3OP).

^{1}HNMR and IR for SB-P2OP: ^{1}HNMR (400 MHz, $CDCl_3$) δ: 0.000 (s, 6H, OSi*(CH$_3$)$_2$*), 0.82407 (s, 9H, SiC*(CH$_3$)$_3$*), 1.533 (s, 9H, N*(CH$_3$)$_3$*), 3.885 (t, 2H, *CH$_2$*CH$_2$OSi), 3.939 (t, 2H, CH$_2$*CH$_2$*OSi), 5.147 (s, 2H, *CH$_2$*-O-C=C-Cl), 6.840 (d, 2H, O-*phenyl*), 7.226 (d, 2H, CO-*phenyl*), 7.636 (s, 1H, N=C-*H*); IR (CH_2Cl_2, cm^{-1}) *v*: 1653 (C=O), 1250 (=C-O-C), 1128 (C-O-C).

^{1}HNMR and IR for SB-P2OP: ^{1}HNMR (400 MHz, $CDCl_3$) δ: 0.000 (s, 6H, OSi*(CH$_3$)$_2$*), 0.828 (s, 9H, SiC*(CH$_3$)$_3$*), 1.568 (s, 9H, N*(CH$_3$)$_3$*), 3.491 - 4.086 (m, 12H, O(*CH$_2$CH$_2$*O)$_3$Si), 5.178 (s, 2H, *CH$_2$*-O-C=C-Cl), 6.880 (d, 2H, O-*phenyl*), 7.258 (d, 2H, CO- *phenyl*), 7.659 (s, 1H, N=C-*H*); IR (CH_2Cl_2, cm^{-1}) *v*: 1643 (C=O), 1248 (=C-O-C), 1131 (C-O-C).

5. Preparation of HB-PnOP (n=1, 3)

Anhydrous tetrahydrofuran (3 mL) was added to the mixture of SB-PnOP (1 equiv) and tert-butylammonium fluoride (4 mmol in 4 mL tetrahydrofuran). After stirring for 2 h, the reaction solution was diluted with ethyl acetate (30 mL), and extracted two times with saturated NaCl solution (30 mL for each extraction). The organic layer was separated and dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was

chromatographed over a column of silica gel and eluted with the mixture of hexane and ethyl acetate = 1 : 3 (v/v). After removal of the solvents under vacuum, HB-PnOP was obtained as yellow oil (yield: 74% for HB-P1OP and 81% for HB-P3OP).

^{1}HNMR and IR for HB-P1OP: ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.531 (s, 9H, N*(CH$_3$)$_3$*), 3.678 (t, 2H, CH_2*CH_2*OH), 3.880 (t, 2H, phenyl-O-CH_2*CH_2*), 4.003 (t, 2H, phenyl-O*CH_2*CH_2), 5.153 (s, 2H, *CH_2*-O-C=C-Cl), 6.855 (d, 2H, O-*phenyl*), 7.245 (d, 2H, CO- *phenyl*), 7.636 (s, 1H, N=C-*H*); IR (CH_2Cl_2, cm^{-1}) *v*: 3363 (O-H), 1645 (C=O), 1248 (=C-O-C), 1146 (C-O-C).

^{1}HNMR and IR for HB-P3OP: ^{1}HNMR (400 MHz, $CDCl_3$) δ: 1.533 (s, 9H, N*(CH$_3$)$_3$*), 3.513 - 4.064 (t, 12H, O(C*H_2*CH_2O)$_3$H), 5.147 (s, 2H, *CH_2*-O-C=C-Cl), 6.854 (d, 2H, O-*phenyl*), 7.230 (d, 2H, CO- *phenyl*), 7.631 (s, 1H, N=C-*H*); IR (CH_2Cl_2, cm^{-1}) *v*: 3449 (O-H), 1649 (C=O), 1248 (=C-O-C), 1122 (C-O-C).

6. Preparation of OTs-PnOP (n=1, 3)

Anhydrous CH_2Cl_2 (10 mL) was added to the mixture of HB-PnOP (1 equiv), TsCl (344 mg, 1.8 mmol, 1.2 equiv), 4-dimethylaminopyridine (219 mg, 1.8 mmol, 1.2 equiv) and N,N-Diisopropylethylamine (233 mg, 1.35 mmol). After stirring for 2 h, the reaction mixture was diluted with ethyl acetate (30 mL), and filtered. The filtrate was washed with 0.1 mol/L HCl (30 mL) and saturated NaCl solution (30 mL). The organic phase was separated and dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was chromatographed over a column of silica gel and eluted with the mixture of hexane and ethyl acetate = 2 : 1 (v/v). After removal of the solvents under vacuum, OTs-PnOP was obtained as yellow solid (yield: 55% for OTs-P1OP and 63% for OTs-P3OP).

^{1}H NMR, ^{13}C NMR, ESI-MS, Elemental analysis, and IR for OTs-P1OP: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.530 (s, 9H, N(C*H$_3$*)$_3$), 2.351 (s, 3H, phenyl-C*H$_3$*), 4.068 (t, 2H, CH_2C*H_2*OS), 4.268 (t, 2H, C*H_2*CH_2OS), 5.132 (s, 2H, phenyl-C*H_2*O), 6.722 (d, 2H, O-*phenyl*), 7.208 (d, 2H, *phenyl*-CH_2O), 7.245 (d, 2H, *phenyl*-CH_3), 7.615 (s, 1H, N=C-*H*),

7.716 (d, 2H, *phenyl*-SO_3); ^{13}C NMR (100 MHz; $CDCl_3$) δ: 21.61, 27.85, 65.57, 66.35, 67.89, 71.66, 115.00, 125.23, 127.68, 127.73, 127.98, 128.92, 129.83, 132.98, 144.95, 153.68, 158.44, 159.01; ESI-MS calculated for $C_{24}H_{27}ClN_2O_6S$: 506.1. Found: 506.5$[M]^+$; Elemental analysis calculated for $C_{24}H_{27}ClN_2O_6S$: C: 56.86%, H: 5.37%, N: 5.53%; Found: C: 56.99%, H: 5.49%, N: 5.67%. IR (KBr, cm^{-1}) v: 1653 (C=O).

^{1}H NMR, ^{13}C NMR, and ESI-MS for OTs-P3OP: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.629 (s, 9H, N(CH_3)$_3$), 2.429 (s, 3H, phenyl-CH_3), 3.602-4.171 (t, 12H, O(CH_2CH_2O)$_3$), 5.242 (s, 2H, phenyl-CH_2O), 6.939 (d, 2H, O-*phenyl*), 7.315-7.336 (t, 4H, *phenyl*-CH_2O), 7.728 (s, 1H, N=C-*H*), 7.792(d, 2H, *phenyl*-SO_3); ^{13}C NMR (100 MHz; $CDCl_3$) δ: 21.66, 27.89, 66.36, 67.53, 68.78, 69.22, 69.75, 70.81, 70.84, 71.82, 115.07, 118.35, 125.30, 127.13, 127.98, 128.97, 129.84, 133.10, 144.80, 153.78, 159.09, 159.24; ESI-MS calculated for $C_{28}H_{35}ClN_2O_8S$: 594.2. Found: 594.6 $[M]^+$.

7. Preparation of nonradioactive [^{19}F]FPnOP (n=1, 3)

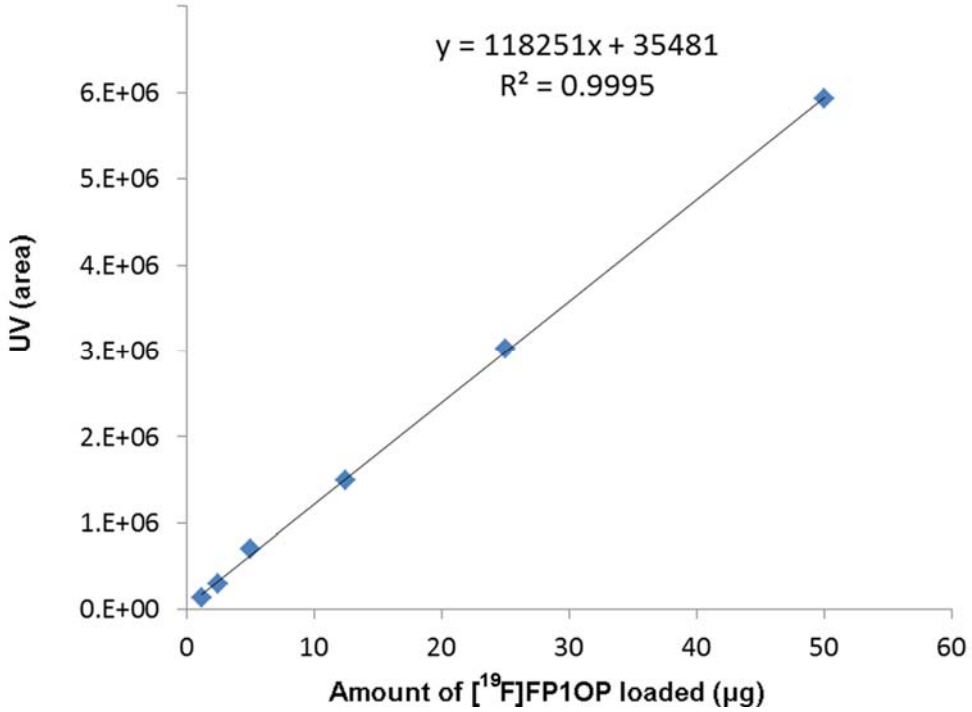
The synthesis route of [^{19}F]FPnOP, shown in Figure 1, is similar as the procedure of [^{19}F]FP2OP[16]. Briefly, the solution of tert-butylammonium fluoride (1 mmol in 1 mL tetrahydrofuran) was stirred in a stream of nitrogen at 110 °C to remove the solvent. Then OTs-PnOP (0.30 mmol in 3 mL anhydrous CH_3CN) was added to the above evaporation residue, and refluxed for 40 min at 90 °C. After concentrated under reduced pressure, the residue was chromatographed over a column of silica gel and eluted with the mixture of CH_2Cl_2 and CH_3OH 100 : 1 (v/v) for [^{19}F]FP1OP, or petroleum ether and ethyl acetate 2 : 1 (v/v). [^{19}F]FP1OP was obtained as white solid (yield: 80%), while [^{19}F]FP3OP was obtained as light yellow oil (yield: 53%).

^{1}H NMR, ^{13}C NMR, ^{19}F NMR, ESI-MS and IR for [^{19}F]FP1OP: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.632 (s, 9H, N(CH_3)$_3$), 4.233 (dt, 2H, CH_2CH_2F), 4.772 (dt, 2H, CH_2CH_2F), 5.256 (s, 2H, CH_2-phenyl), 6.965 (d, 2H, O-*phenyl*), 7.353 (d, 2H, *phenyl*-CH_2O), 7.730 (s, 1H,

N=C-*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ: 27.85, 66.33, 67.22 (d, J = 20 Hz), 71.73, 82.76 (d, J = 170 Hz), 115.08, 118.39, 125.31, 127.58, 128.97, 153.73, 158.86, 159.03; ^{19}F NMR δ: -223.85; ESI-MS calculated for $C_{17}H_{20}ClFN_2O_3$: 354.1. Found 355.2 $[M+1]^+$; IR (CH_2Cl_2, cm^{-1}) v: 1645 (C=O), 1249 (=C-O-C), 1095 (C-O-C).

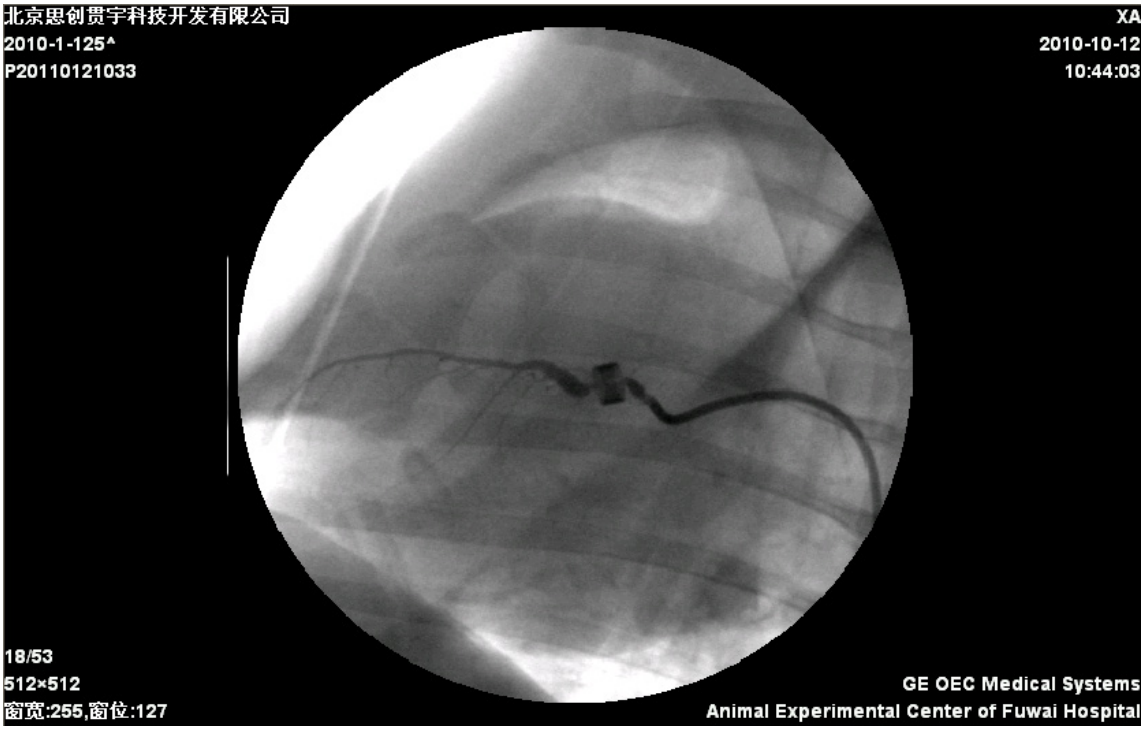
^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and ESI-MS for [^{19}F]FP3OP: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.629 (s, 9H, N(CH_3)$_3$), 3.698-4.628 (m, 12H, F(CH_2CH_2O)$_3$), 5.243 (s, 2H, CH_2-phenyl), 6.952 (d, 2H, O-*phenyl*), 7.324 (d, 2H, *phenyl*-CH_2O), 7.715 (s, 1H, N=C-*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ: 27.87, 66.32, 67.54, 69.74, 70.45 (d, J = 19 Hz), 70.86, 70.88, 71.81, 83.12 (d, J = 168 Hz), 115.04, 118.27, 125.33, 127.09, 128.94, 153.78, 159.07, 159.24; ^{19}F NMR δ: -222.89; ESI-MS calculated for $C_{21}H_{28}ClFN_2O_5$: 442.2. Found 442.6 $[M]^+$.

8. The HPLC quantitative analysis of [^{19}F]FP1OP in solution for specific activity calculation. The relationship between UV area of HPLC and the mass of [^{19}F]FP1OP loaded is shown in below:



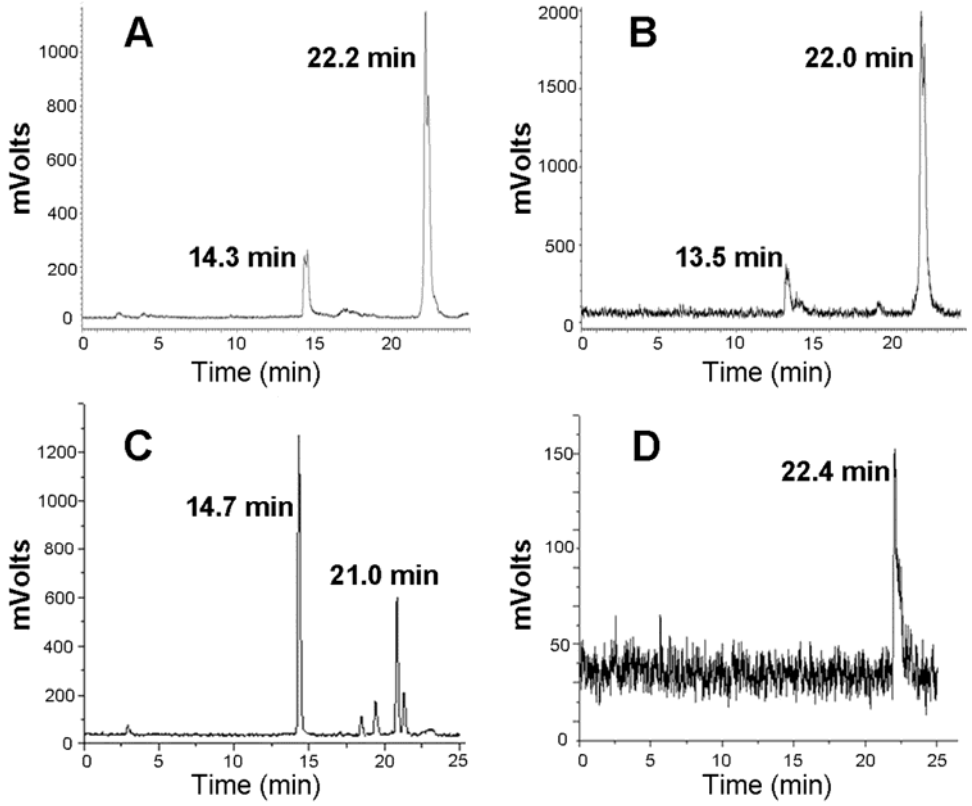
Supplemental Figure 2. Standard curve for quantitative analysis of [^{19}F]FP1OP by HPLC

9. CT coronary angiography



Supplemental Figure 3. The chronic myocardial ischemia model was confirmed by CT coronary angiography after PET/CT imaging.

10. The HPLC profiles of stability study



Supplemental Figure 4. The radiochromatograms of [^{18}F]FP1OP after storage in water at room temperature for 1 h, about 85% of the total ^{18}F was eluted at 22.2 min (A), in murine plasma at 37 °C for 1 h, about 80% of the total ^{18}F was eluted at 22.0 min (B) and [^{18}F]FP3OP after storage in water at room temperature for 1 h, about 24% of the total ^{18}F was eluted at 21.0 min (C), and [^{18}F]FP1OP after storage in 80% ethanol solution at room temperature for 4 h, over 95% of the total ^{18}F was eluted at 22.4 min (D).

11. Statistical analysis and determination of LD_{50}

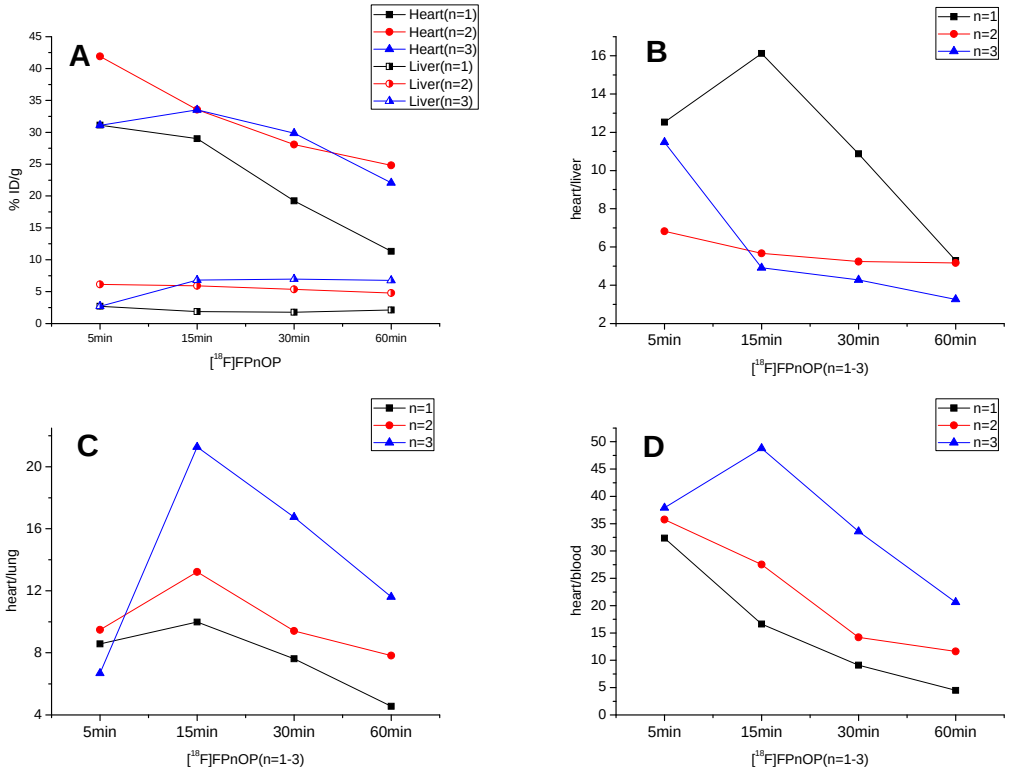
LD_{50}, based on mortality data, were calculated according to the Bliss method (Bliss, C. I.: The determination of the dosage-mortality curve from small numbers. Quart. J. Pharm. and Pharmacol., 11, 192-216, 1938) at a 95% confidence.

Supplemental Table 1. Lethality after injection [^{19}F]FP1OP through tail vein

Dose (mg/kg)	1.6043	1.383	1.2171	1.1064	1.0142	0.0000
Lethality *	8/10	7/10	4/10	3/10	1/10	0/10

* Dead animals/treated animals.

12. The comparison of three ^{18}F-labeled pyridaben analogues with different length of side radiolabeling chain in biodistribution study. The data of [^{18}F]FP2OP were published previously (Mou T, Jing H, Yang W, et al. Preparation and biodistribution of [^{18}F]FP2OP as myocardial perfusion imaging agent for positron emission tomography. *Bioorganic & Medicinal Chemistry.* 2010;18(3):1312-1320).



Supplemental Figure 5. Comparison of myocardium and liver uptake of [^{18}F]FPnOP (n=1-3) at time points of 5, 15, 30, 60 minutes after injection in mice (A). Results are expressed as percent of injected dose per gram (%ID/g). Comparison of uptake ratios of heart to liver (B), lung (C), and blood (D) at 5, 15, 30, 60 minutes after [^{18}F]FPnOP (n=1-3) administration in mice.